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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/809,060 | 03/25/2004 | Heinz-Gerd Klaes | 1/1475 | 7001 |

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| EXAMINER | |
|---|---|
| LEWIS, PATRICK T | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | |

DATE MAILED: 10/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/809,060 | KLAES ET AL. | |
| | Examiner | Art Unit | |
| | Patrick T. Lewis | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-41 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-41 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 02142005.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions and kits useful for treating HIV or hepatitis B virus wherein the pharmaceutical composition comprises tipranavir and at least one antiviral active compound of formula (I) wherein said compound is selected from the group consisting of 3'-deoxy-3'fluorothymidine (FLT), 2',3'-dideoxyfluoroguanosine (FLG), 3'-deoxy-3'-fluoro-5-O-[2-(L-valyloxy)-propionyl]guanosine, and pharmaceutically acceptable salts or prodrugs thereof and for methods for the treatment of HIV or hepatitis B virus in a patient comprising administering tipranavir and at least one antiviral active compound of formula (I) wherein said compound is selected from the group consisting of 3'-deoxy-3'fluorothymidine (FLT), 2',3'-dideoxyfluoroguanosine (FLG), 3'-deoxy-3'-fluoro-5-O-[2-(L-valyloxy)-propionyl]guanosine, and pharmaceutically acceptable salts or prodrugs thereof does not reasonably provide enablement for pharmacological compositions and kits useful for the treatment or prophylaxis of viral infections broadly or methods for the treatment or prophylaxis of viral infections broadly. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

1. the breadth of the claims;
2. the nature of the invention;
3. the state of the prior art;
4. the level of one of ordinary skill in the art;
5. the level of predictability in the art;
6. the amount of direction provided by the inventor;
7. the existence of working examples; and
8. the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

**Breath of Claims**

The instant claims are drawn to 1) a pharmaceutical composition useful for the treatment of prophylaxis of viral infections comprising tipranavir and at least one antiviral active compound of formula (I), 2) a method for the prophylaxis or treatment of a viral infection in a patient comprising administering tipranavir and at least one antiviral active compound of formula (I), and 3) a kit of parts for the prophylaxis or treatment of a viral infection in a patient comprising a first containment containing a pharmaceutical

composition comprising tipranavir and at least one pharmaceutically acceptable carrier and a second containment containing a pharmaceutical composition comprising an antiviral active compound of formula (I). One of ordinary skill in the art would not be apprised of the metes and bounds of compounds of formula (I) in the absence of a chemical name or distinctly set forth chemical structure.

**Nature of Invention**

The invention relates to compositions and methods useful for the treatment and prophylaxis of viral infections.

**State of the Prior Art**

Hirschman US 2001/0036920 A1 (Hirschman) is representative of the prior art at the time of the invention. Hirschman teaches that the treatment of viral diseases in humans is a major focus of medical science (page 1). While some progress has been made, viral infections are still among the diseases most difficult to treat. Despite growing understanding of viral diseases along with improved techniques for detecting and treating them, few antiviral drugs have proved effective. Further, new viral diseases constantly appear as an inevitable consequence of evolution. Thus, searching for a novel and effective way of treating viral diseases remains imperative and challenging. In developing an antiviral agent, it is well known that inhibitory activity of an antiviral agent against a particular virus cannot be equated with its inhibitory effect against another virus. For example, acyclovir has proved to be specifically effective against herpes simplex 1 and 2 but not against cytomegalovirus (CMV), even though both HSV and CMV belong to the same herpesvirus family, sharing certain genetic features.

Without the knowledge of a virus' genetic traits and the chemical properties of an antiviral agent, treatment of a viral infection becomes unpredictable.

**Level of Ordinary Skill in the Art**

The level of ordinary skill in the art is seen to be a M.D. experienced in the treatment of viral infections or a PhD in the field of biomedical research.

**Level of Predictability in the Art /Amount of Direction Provided by the Inventor**

Please note that a single embodiment may provide broad enablement in cases involving predictable factors, but more is required in cases involving unpredictable factors, such as chemical or physiological activity, see *Ex. parte Hitzeman*, 9 USPQ2d 1821. In the instant case, no experimental data or citations of relevant prior art are presented in support of applicant's assertion that the treatment or prophylaxis of the vast number of viral infections is accomplished by administering a patient tipranavir and at least one compound of formula (I). The prior art (Hirschman) that without the knowledge of a virus' genetic traits and the chemical properties of an antiviral agent, treatment of a viral infection becomes unpredictable. Additionally, the instant specification provides no guidance as to how the skilled artisan would address various factors of concurrent co-administration of tipranavir and a compound of formula (I). Such factors include but are not limited to:

1. determination of the effects of the combination of drugs as they relate to their collective primary action chemically,

2. determination of the chemical properties of the combination of drugs (e.g., regarding collective interaction with cell receptors, toxicity, absorption), and

3. determination of the physical or structure-activity relationship between the combination of the active ingredients including cellular sites of drug action and modification of the active ingredients.

**Working Examples**

There are no working examples in the instant specification.

**Quantity of Experimentation Needed to make and/or use the Invention Based on the Content of the Disclosure**

When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation. In the instant case, the phrase "for the treatment or prophylaxis of viral infections" limits the composition/kit. There are no teachings in the prior art suggesting the broad treatment of prophylaxis of viral infections using a single composition of particular treatment regimen. Applicant has not provided any working examples. As such, a skilled artisan would not recognize that a combination of tipranavir and a compound of formula (I) is useful in the treatment of prophylaxis of viral infections as broadly claimed.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 5-21, 25-34 and 38-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The chemical structure representing compounds of formula (I) is indefinite. The structure contains bonds connected to the ribose ring; however, it is unclear what atoms

or moieties are connected to the other end of the bond. One of ordinary skill in the art would not be apprised as to whether applicant intends the absent moieties to be limited to H or a methyl group or if applicant intends that a limitless number of moieties are suitable

5. Claims 4, 24 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4, 24 and 37 recites the limitation "wherein the compound of formula (I) is 3'-deoxy-3'-fluoro-5-O-[2-(L-valyloxy)-propionyl]guanosine". There is insufficient antecedent basis for this limitation in the claim. The independent claim limits the 5'-position to a hydroxyl group.

6. Claims 5, 8, 10-20, 25-28, 32, and 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "synergistic ratio", "a further NRTI", "non-nucleoside reverse transcriptase inhibitor", "entry inhibitor", "integrase inhibitor", "a further nucleoside reverse transcriptase", "PA-457", "KPC-2", "HGTV-43", "AG-1776", "AG-1859", "DPC-681/684", "GS224338", "KNI-272", "Nar-DG-35", "P(PL)-100", "P-1946", "R-944", "RO-0334649", "TMC-114", "VX-385", and "VX-478" have not been defined in the claims or specification. There is nothing inherently wrong with defining some part of an invention in functional terms; however, a functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary

skill in the pertinent art in the context in which it is used. Functional descriptions of chemical compounds/compositions must be coupled with a known or disclosed correlation between function and structure.

***Conclusion***

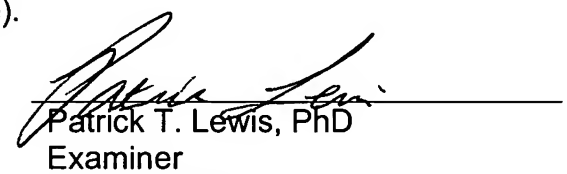
7. Claims 1-41 are pending. Claims 1-41 are rejected. No claims are allowed.

***Contacts***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Patrick T. Lewis, PhD
Examiner
Art Unit 1623

ptl